

End-Stage Renal Disease (ESRD): Physical Activity and Elucidation of Its Effects on Biochemical and Haematological Parameters in Haemodialysis Patients

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Abstract

End-stage renal disease (ESRD) is a progressive disorder for which there is no prospect of recovery, and for which patients receive regular haemodialysis. In ESRD the ability of the kidneys to excrete metabolic waste products and to regulate the composition of extracellular fluid is compromised. Symptoms of ESRD also include cardiovascular dysfunction, anaemia, malnutrition, muscle wasting, muscle weakness, glucose intolerance and reduced bone density. Patients with ESRD are likely to be challenged by participation in exercise whilst undergoing a HD regimen. Nevertheless there is a case for prescribing exercise in patients who struggle to become active. Some benefits of exercise in patients receiving haemodialysis, the benefits of physical exercise, which include: 1) Reduction of toxins and fluid overload in the circulatory system, permitting improved tolerance to the HD regimen and 2) Increased heart rate, which improves cardiovascular performance, 3) a reduction in comorbidities and an increase in well-being, and 4) the facilitation of positive coping strategies. An understanding how exercise can be of clinical advantage in ESRD patients is unique and challenging given the variety of nutritional and clinical conditions with which they present. The haematological and biochemical parameters which should be monitored in these patients (including blood potassium, urea, calcium and hemoglobin levels) need to be prioritized, and this prioritization depends in turn upon general patient well-being. More research is also required in the understanding of physiology and importance of good nutrition in this population. The aim of this work is to provide some background of the key parameters in HD patients and to identify literature on biochemical parameters which are affected during physical activity in HD patients. The results help to emphasize that closer attention should be paid to monitoring HD efficacy and Kt/V, a measure of dialysis adequacy.

Keywords: Nephrology; Physical activity; Haemodialysis; Chronic kidney disease; Kt/v

Introduction

Haemodialysis (HD) is a form of renal replacement therapy (RRT) as is continuous ambulatory peritoneal dialysis (CAPD). Although different in their protocols, both forms of treatment allow a steady-state of clinical biochemical and haematological parameters [1]. These include creatinine, urea, sodium, calcium, and other important components. It should be acknowledged; patients who have poor treatment efficacy (identified using Kt/V measurement) will feel worse over time. Physical activity may be an important factor in dialysis adequacy/efficiency (be it short-term or long-term) and in preparation for patients awaiting a transplant.

It is known that vigorous physical activity (particular intense cardiovascular workout) has many benefits. Some of the parameters that are affected include: β -endorphin, reduced urea, and positive psychology. These all benefit in the preparation to transplantation. However, at present there is little evidence that collaborates physical activity, stress and the parameters that are/should be monitored closely in the HD population; more efforts are being made to interrogate exercise literature (or physical activity research) and renal health. One study used two groups of athletes [1]. One of these groups represented subjects with a range of fitness levels from recreational to high-performance running. The second group represented canoeists with a similar range of fitness levels. The study measured the *in vitro* responses of leukocytes following acute anaerobic exercise over a 24 h recovery period. There was a reduction in proliferative lymphocyte response which was shown to be brief and transient. Other research investigating how physical activity effects specific immunological parameters demonstrated that prolonged endurance exercise causes an increase in plasma levels of interleukin-1 (IL-1), possibly as a response to muscle injuries, but plasma interleukin-2 levels were generally reduced [2]. IL-1 secretion may enhance the responsiveness of peripheral blood mononuclear cells, but prostaglandin secretion decreases their IL-2 production. The observations may have been due to altered IL-2 levels or IL-2 receptor expression. In this study, appropriately graded physical activity reduces the adverse immune reactions associated with challenging exercise. This study gives general information relating to lymphocyte migration during exercise [3]. Work has

also informed how through the immune system, transplantation and psychological stress, some biochemical parameters are more affected than others [4].

Aim of this Work

This work aims to provide some background on key haematological and biochemical parameters which are measured in HD patients, and in addition to identify literature on biochemical parameters specifically influenced by physical activity in HD patients. I will conclude that closer attention to monitoring HD efficacy and Kt/V is needed.

General Benefits of Physical Activity in HD Patients

It has been documented that physical activity as measured by peak oxygen uptake is generally low in HD patient groups [5-9]. There are a number of factors that may contribute to this, including anaemia, cardiac dysfunction (reduced contractility and increased preload and afterload of ventricular muscle), vascular dysfunction (a limitation in the capacity to divert cardiac output to skeletal muscle), skeletal muscle abnormalities (reduced fibre size, capillary density, mitochondrial density/function, increased diffusion distance) and/or metabolic abnormalities and autonomic nervous system dysfunction [10-17]. At the same time, physical activity has the following benefits in HD patients: Some benefits of exercise in HD patients include: 1) Reduces toxins in the blood and fluid overload, thus allowing patients to tolerate HD regimen better and 2) Exercise increases heart rate, which in turn also allows increases strength to cardiovascular system, 3) Because of the increased heart rate during exercise/physical activity, this will in turn allow an increase blood flow through vascular system (fistulae access, especially), which then means patients would get better Kt/V results overall, 4) Exercise will reduce the amount of fluid to come off during HD, 5) Exercise causes an increase in β -endorphin hormone, which causes a state of 'feeling good'-this in turn prompts a positive mental attitude despite overwhelming circumstances, 5) A long-term physical activity protocol (2-3 times a week) in HD patients may be one of the best ways for the body to prepare for a renal transplant [4]. Exhaustion post exercise generally causes a period where there is an activated immune response. This is not necessarily the same immune response as evident during a cold or an infection or even post transplantation. This is because during bouts of intense exercise, there is secretion of β -endorphins and 6) Exercise can aid to cope with traumatic procedures such as fistulae and other forms of access creation [4].

Physical Activity in Post-Transplant Patients

Post-transplant CKD patients cannot participate in exercise to the same extent as in normal patients, and this is expected because they are at higher risk of cardiovascular

disease [5-8]. Research suggests an association between higher physical activity levels and slower rate of estimated glomerular filtration rate (eGFR) loss in patients with CKD stages 3 and 4 [9]. Experimental interventions to improve cardiovascular risk factors or renal function by increasing exercise capacity in patients. In post-transplant patients, procedures and protocols differ from the HD patient. The most challenging period post-transplant is the initial 3-6 months, where the immune system is adapting/or tolerating the 'new' organ. For many patients this period is stressful and strenuous. The initial phases post-transplant involves 'constant' observation of creatinine (being the main clinical parameter); in addition to ensuring the immunosuppression dosage/titres are correct. A renal biopsy is quite common in early post-transplant and this brings on various additional emotions [4]. Exercise is recommended (but not prescribed) in the 'late' post-transplant period, where clinical chemistry parameters are less susceptible to 'blips'. Exercise generally improves coping, regardless of whether on an HD regime or transplanted. Patients who exercise 'later' post-transplant will also have reduced episodes of stress, depression and frustration. Physical activity may also indirectly aid to reduce episodes of AAR [4] because increase blood flow through afferent and efferent arterioles of the kidneys.

Biochemical Parameters in HD Patients

Urea

Urea is a small molecule produced from protein and it is excreted by the kidneys in normal renal function; when renal function declines, urea levels rise [16,18]. It is synthesized by the reactions of the urea cycle from carbamoyl phosphate and ammonium ions, the latter being derived from deamination reactions [16,18]. It is not such an accurate test for kidney function as creatinine, but is a useful test when used together with creatinine, because it is affected by muscle breakdown, how much protein consumed and whether a patient has consumed enough fluid (it rises if dehydrated). The normal range=2.5 mmol/l to 7.1 mmol/l (7-20 mg/dl) [16,18].

Potassium

Potassium is important for cellular/interstitial fluid balance and for normal function of the heart, kidneys and other organs. A diet includes fruit (notably bananas), vegetables and protein provides the normal daily allowance of potassium. Potassium is also available in supplements, but the intake of too much potassium can be harmful, especially for people with renal disease or those taking some drugs to treat hypertension [16,18]. Potassium is critical for maintaining the normal electrical rhythm of the heart and nerve impulses. The normal potassium level in the blood is 3.5 mEq/L to 5.0 mEq/L (milli Equivalents per liter). Potassium levels between 5.1 mEq/L to 6.0 mEq/L are considered to represent mild hyperkalemia [16,18].

Calcium

There is a broad normal physiological range of total and free Calcium concentrations, depending on age, sex, physiological state (e.g. pregnancy), combined with seasonal variations which follow a variation in the blood level of vitamin D, directly involved in the regulation of calcium concentration [16,18]. In HD patients, calcium and phosphate mineral metabolism is compromised owing to the attribute renal insufficiency and decline in renal function. The corrected total serum calcium concentration is normally 8.5 mg/dL to 10.2 mg/dL, but there is no absolute reference point for serum calcium levels either in hypocalcemia or hypercalcemia, at which adverse symptoms will occur [16,18]. **Table 1** provides a summary of clinical biochemical variables obtained from the UK Renal Registry (UKRR).

Table 1 A summary of clinical biochemical variables.

Biochemical Variable	Clinical Audit Measure	Conversion Factor from SI Units
Phosphate	HD Patients: 1.1-1.7 mmol/l	Mg/dl=mmol/l × 3.1
	PD Patients: 1.1-1.7 mmol/l	
Calcium (adjusted)	Normal range (<2.5 mmol/l)	Mg/dl=mmol/l × 4
Parathyroid hormone	2-9 times upper limit of normal	Mg/dl=mmol/l × 9.5
Bicarbonate	HD Patients: 18-24 mmol/l	Mg/dl=mmol/l × 6.1
	PD Patients: 22-30 mmol/l	
Ref: Table adapted from [19]		

Relevance of Kt/V

Kt/V is used to measure the effectiveness of HD treatment, and involves the measurement of blood urea before and after treatment, to show how much toxin has been removed from the blood. URR is a simpler test of HD effectiveness: some units use URR, some use Kt/V, some use both. In the UK the accepted target for Kt/V is a minimum of 1.2, (the optimum target is between 1.6 and 1.8+) [18]. A slightly lower value may be acceptable if a patient has some renal function (eGFR=15%+). Lower values are associated with a poorer HD poorer prognosis. If HD patients exercise, the majority of clinical chemistry parameters will stay stable; this ultimately enhances HD efficiency [18]. **Table 2** summarizes how patients can achieve higher Kt/V values.

It must be noted that not all patients will be able to achieve high Kt/V results owing to pre-determined vascular complications.

Importance of Creatinine in HD patients

Effectively, creatinine is a by-product of muscle break-down. Because a majority of recipients on HD and CAPD do not have relative renal function, the creatinine will stay above the

normal range (60 mmol/l to 120 mmol/l or 0.7 mg/dl to 1.4 mg/dl). The creatinine will not necessarily be of significant difference when compared to a patient who has been transplanted, simply because regardless of HD efficacy, the quantity of blood processed/replenished is limited in comparison to the function of a native kidney/transplant. Creatinine is thus not specifically an important biomarker for renal function in HD patients; however it is important for muscle mass which is why protein is also important in these patients because it strengthens cardiac muscle and body mass [18].

Table 2 How patients can achieve higher Kt/V results.

Increasing HD Efficiency
Large gauge/Barrel needles post fistulae maturation
4.5 hours; 3 times a week
Good spread of needles across access
Increased dialysate flow (600mls/min to 700 mls/min)
Physical activity in between or during HD treatment
Ref: Table adapted from [20]

Haematological Parameters in HD Patients

In ESRD, serum free iron concentration, and iron-saturation of transferrin, and ferritin are usually normal. Non-heme iron absorption from the gut is also normal. This has been observed in detailed studies on iron kinetics, where it has been proposed that, in view of the increased levels which can occur in response to acute anaemia or hypoxic hypoxia in ESRD patients, a decoupling between the endocrine and the excretory function of the kidney is responsible rather than its inability to produce erythropoietin [21].

The improvement in anaemia symptoms after starting haemodialysis was first described in 1970. It was postulated that this was due to the presence of the uremic inhibitors of erythropoiesis in the plasma. Polar lipids, arsenic, spermine and spermidine, vitamin A, and the parathyroid hormone are possible sources of uremic inhibition. Aluminium overload in haemodialysis patients is also proposed to cause microcytic anaemia, probably by inhibiting erythroid marrow as a result of binding to transferrin [22,23]. Blood loss, amounting to 4 ml to 20 ml, is associated with the dialysis procedure, with additional loss resulting from frequent blood sampling. As a result a patient who is on dialysis may lose in excess of 2 mg of iron per day. In addition, chronic infection and chronic inflammation may play a major role in the pathogenesis of anaemia [23]. One study has identified apparent microcytic hypochromic anaemia in HD patients [24] and another has revealed normocytic normochromic anaemia in 81% of HD patients [25]. The pathogenesis of uremic bleeding is not fully understood. No major alterations of the plasma coagulation factors have been reported, and the fibrinolytic system does not appear to be impaired. The common haematological

manifestations of uremia are ecchymosis, purpura, epistaxis, and bleeding from venopuncture sites. Cardiac tamponade following pericarditis and pleural effusion can also occur. Spontaneous sub-capsular haematoma of the liver is a major complication, as are subdural haematomas. Uremic bleeding has also been attributed to a quantitative platelet reduction in 20% to 52% of the cases [26,27]. The exact mechanism behind the elevated erythrocyte sedimentation rate (ESR) in ESRD is not clear. **Table 3** provides a summary of haematology in ESRD patients.

Table 3 A summary of haematological concerns in ESRD patients.

Anaemia
Reduced erythropoietin
Aluminum excess
Anaemia of Chronic Disorders
Iron Deficiency-Blood loss, e.g. venesection, defective platelet function
Folate deficiency-Chronic HD without replacement therapy
Abnormal Platelet Function
Thrombocytopenia
Immune complex-mediated, e.g. systemic lupus erythematosus (SLE)
Polyarteritis nodosa (PN)
Some cases of acute nephritis following allograft
Hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP)
Thrombosis
Some cases of nephrotic syndrome (NS)
Polycythemia
In renal allograft recipients
Rare in renal cell carcinoma, cysts, arterial disease
Ref: Table adapted from [28]

Physical Activity in Renal Patients

One study observed 18 HD patients, 12 continuous ambulatory peritoneal dialysis (CAPD) patients and 20 post-transplant patients performed maximal treadmill exercise tests. Heart rates and blood pressures were determined every minute and maximal oxygen consumption was measured directly [28]. Exercise capacity as measured by VO_2 max is low in HD patients and is similar to inactive untreated renal transplant patients. Maximal heart rates were significantly lower in haemodialysis patients than transplant recipients. The lower exercise tolerance in end-stage renal disease (ESRD) indicates that most patients regardless of the treatment mode could benefit from attempts through exercise training to increase physical working capacity [29].

Another investigation explored the effects in uremic patients of handgrip exercise on plasma catecholamine levels,

neuropeptide-Y (NPY), and leu-enkephalin before and after HD [30]. In this study dopamine levels were higher in the uremic group before than after HD treatment both during rest ($0.38 \text{ pmol/ml} \pm 0.39 \text{ pmol/ml}$ and handgrip exercise $1.13 \text{ pmol/ml} \pm 1.00 \text{ pmol/ml}$ compared to controls $0.17 \text{ pmol/ml} \pm 0.19 \text{ pmol/ml}$, and $0.66 \text{ pmol/ml} \pm 0.83 \text{ pmol/ml}$). HD treatment led to further increase in dopamine $0.49 \text{ pmol/ml} \pm 0.35 \text{ pmol/ml}$ at rest. Noradrenaline levels were almost the same in uremic patients before $0.43 \text{ pmol/ml} \pm 0.51 \text{ pmol/ml}$ and after dialysis $0.46 \text{ pmol/ml} \pm 0.60 \text{ pmol/ml}$ as in control subjects $0.41 \text{ pmol/ml} \pm 0.37 \text{ pmol/ml}$ during rest. The level measured after the handgrip was the highest in the uremic group after dialysis $2.10 \text{ pmol/ml} \pm 2.00 \text{ pmol/ml}$, significantly lower before dialysis $1.26 \text{ pmol/ml} \pm 0.85 \text{ pmol/ml}$, and the lowest in control group $0.78 \text{ pmol/ml} \pm 0.43 \text{ pmol/ml}$ [30]. Noradrenaline levels were very similar in the uremic group before dialysis ($1.54 \text{ pmol/ml} \pm 1.05 \text{ pmol/ml}$, after dialysis $1.79 \text{ pmol/ml} \pm 1.29 \text{ pmol/ml}$ and in the control group $1.46 \text{ pmol/ml} \pm 1.06 \text{ pmol/ml}$) at rest. During the handgrip test its level was higher in uremic group after HD than before it (adequate values $8.78 \text{ pmol/ml} \pm 4.61 \text{ pmol/ml}$ and $6.70 \text{ pmol/ml} \pm 4.74 \text{ pmol/ml}$). The difference between uremia group before dialysis and control group did not reach significance. The level of NPY has the tendency to increase in uremic patients. HD leads to following increase of its level, but the changes did not reach the significance both in rest and handgrip. Leu-enkephalin level was higher in uremic group ($9.21 \pm 7.62 \text{ pmol/ml}$) compared to control group ($5.22 \pm 1.53 \text{ pmol/ml}$). The team identified that there was a non-significant fall of this parameter post HD ($6.79 \pm 4.76 \text{ pmol/ml}$). This team established that uremia leads to increase the level of dopamine and Leu-enkephalin during rest and handgrip, but the level of epinephrine only during the handgrip. HD treatment led to further increase of dopamine during rest, but epinephrine, norepinephrine and Leu-enkephalin only during handgrip exercise [30].

Physical Activity in CAPD Patients

In a study on exercise tolerance, blood biochemistry, blood pressure (BP) control, cardiac function, and quality of life (QOL) over a 12-week exercise program [31], scores were calculated from 13 patients undergoing continuous ambulatory peritoneal dialysis (CAPD; six men and seven women of mean age, 46.5 ± 12.8 years, and with a mean duration of dialysis of 4.8 ± 3.8 years). The patients underwent exercise training using treadmill running or cycling with arm ergometers three times a week. Seven CAPD patients who were matched for age, sex, and duration on dialysis served as controls.

The mean peak aerobic capacity (VO_2 peak) of the patients increased by 16.2% after training (pre- and post-exercise, $17.2 \pm 5.2 \text{ mL/kg/min}$ v $20.0 \pm 6.4 \text{ mL/kg/min}$; $P=0.004$) [31]. Although there were no significant changes in serum urea, creatinine, albumin, hematocrit levels, left ventricular diastolic/systolic diameter ratio and ejection fraction, an increasing trend in plasma high-density lipoproteins (HDLs) was observed (baseline vs. post exercise, $33 \pm 11 \text{ mg/dL}$ v $40 \pm$

14 mg/dL; $P=0.06$). Twenty four hour ambulatory BP monitoring indicated a significant increase in daytime systolic BP (pre- and post-exercise, 142 ± 26 mmHg v 157 ± 22 mmHg; $P=0.003$), but no significant changes could be found in the ambulatory daytime diastolic BP, nocturnal BP, and resting clinic BP. The patients' QOL improved after training, with better scores in two of the kidney disease quality of life scales (KDQOL): burden of kidney disease and physical functioning. Two mild and uncomplicated hypotensive episodes were reported in two patients immediately after training. No changes occurred in exercise capacity, blood biochemistry, BP profile, and QOL scores in the controls. The team concludes that structured aerobic exercise is safe and can improve the exercise tolerance and QOL outcomes in CAPD patients [31]. Another study investigated factors that influence peak VO_2 in patients receiving CAPD [32]. The study included 22 ESRD patients (12 men, 10 women; ages 29.64 ± 8.29 years; CAPD duration, 37.35 months ± 7.15 months). The results suggested that low physical activity might be related to serum phosphorus levels, and that optimal control of serum phosphorus therapy would increase exercise capacity, duration, and oxygen consumption; resulting in a decrease of post-operative mortality in renal transplant candidates [32].

Physical Activity in HD Patients

In further work to determine the effects of physical activity on left ventricular function at rest and during sub maximal effort, thirty-eight ESRD patients maintained on HD were recruited and randomized into three groups [31]. Sixteen patients (Group A - mean age 46.4 ± 13.9 years, without clinical features of heart failure) participated in a 6 month renal rehabilitation program with supervised exercise consisting of three weekly sessions of aerobic training. A further ten patients (Group B - mean age 51.4 ± 12.5 years) followed a moderate exercise program at home. A final group of twelve (Group C - mean age 50.2 ± 7.9 years) were not trained and remained as controls. The level of anaemia and the HD prescription remained constant in all groups during the study [33]. A healthy control group comprised fifteen sex- and age-matched inactive individuals (Group D - mean age 46.9 ± 6.4 years) were the healthy controls. All patients at the start and end of the program underwent physical examination, laboratory tests, treadmill exercise testing, M-mode and 2-D echocardiograms performed at rest and at peak of supine bicycle exercise. Left ventricular volumes (EDV, ESV) and mass (LVM) were measured and ejection fraction (EF), stroke volume index (SVI) and cardiac output index (COI) were calculated using the standard formulae. The maximal oxygen consumption increased by 43% ($P=0.001$) and the exercise time by 33% ($P=0.001$) after training in group A, by 17% ($P=0.001$) and 14% ($P=0.01$), respectively, in B, and both remained unchanged in Group C. Training in Group A was also associated with an increase in LVIDd (from 52.1 ± 6.4 mm to 54.0 ± 6.1 mm, $P=0.001$) and LVM (226 ± 67 g to 240 ± 84 g, $P=0.05$) at rest with no change noted in Groups B and C. Following a 6 month exercise training in Group A, an increase was also found in the resting EF by 5% ($P=0.01$) and SVI by 14% ($P=0.001$). There were no changes in these parameters in

Groups B and C [33]. Supine bicycle exercise after training in Group A was associated with an improvement in EF by 14% compared to the pre-training change ($P=0.001$), SVI increased by 14% ($P=0.001$) and COI by 73% ($P=0.001$). There were similar but less pronounced changes from rest to sub maximal exercise in Group B following training at home. The untrained patients showed no changes in LV systolic function over the 6 month period. The study demonstrated that intense exercise training improves LV systolic function at rest in HD patients; both intense and moderate physical activity led to enhanced cardiac performance during supine sub maximal exercise [33].

Another study investigated when physical activity can reduce urea, creatinine, and potassium during HD [34]. Eleven patients (aged 32-78 years) on HD (4-58 months duration) were studied on paired HD sessions; one with exercise and the other as a control. Patients cycled for 5-20 min at sub maximal workload, and the exercise was followed by 10 min rest to achieve a total 60 min exercise period. Plasma concentrations of urea, creatinine and potassium were measured pre-, post- and 30-min post HD. The post-dialysis rebound (% rebound) and reduction ratios (RR) of the solutes and equilibrated (two-pool) urea and Kt/V were calculated for comparison [34]. Results demonstrate rebounds of all three solutes were reduced following exercise. The rebound of urea decreased from 12.4% to 10.9% (median, $P=0.01$; Wilcoxon signed rank test), creatinine from 21.2% to 17.2% ($P=0.001$) and potassium from 62% to 44% ($P=0.05$). Kt/V and RR increased significantly as a result: Kt/V urea from 1.00 to 1.15 ($P=0.001$), RR urea from 0.63 to 0.68 ($P=0.001$); Kt/V creatinine from 0.71 to 0.84 ($P=0.01$); and RR creatinine from 0.51 to 0.57 ($P=0.05$). From the results it was concluded that exercise increased the efficiency of HD by reducing the rebound of solutes due to increased perfusion of the skeletal muscle [34].

Physical Activity and HD Adequacy

A further study investigated the effect of exercise on HD adequacy [35]. Twenty (20) studies were performed in 20 maintenance HD patients. An adapted exercise cycle was attached to the dialysis bed. The patients in exercise group pedaled throughout dialysis, and had a 5-10 minutes rest if they needed, while the patients of a control group had no exercise. Blood, urea and nitrogen (BUN), serum creatinine (SCr) and urea were measured just before and after HD immediately, and 60 minutes post HD. In the exercise group, after HD, both BUN and SCr rates were shown to be significantly higher, whilst the rebound of BUN, SCr and Urea were significantly lower than those in the control group ($P<0.05$, approximately 0.01). Kt/V was also higher in the exercise group ($P<0.05$, approximately 0.01). The results showed that exercise during HD is a practical new way to improve the dialysis adequacy [35].

Physical training is being recommended as a complementary therapeutic approach [34]. This is supported by a study in which three methods of exercise training were evaluated in patients with ESRD: These were (1) a supervised outpatient programme that is held in a rehabilitation center; (2) a home exercise rehabilitation programme; and (3) an exercise

rehabilitation programme undertaken during the first few hours of the HD treatment in a renal unit. Training data show that the application of an exercise training programme in patients with ESRD enhances their physical fitness. This improvement is due to central and mainly peripheral adaptations [36]. Physical activity training in HD patients increases aerobic capacity, causes favorable left ventricular functional adaptations, reduces blood pressure in patients with hypertension, modifies other coronary risk factors, increases the cardiac vagal activity and suppresses the incidence of cardiac arrhythmias. Moreover, physical training has beneficial effects on muscle structural and functional abnormalities [36]. The study established that central and peripheral adaptations to training cause an increase in their functional capacity and offer them a better chance of coping. Moreover, physical activity improves exercise tolerance of renal post-transplant patients [36].

Physical Activity and Health Perception

A further study investigated the effects of 2 methods of long-term physical training on physical fitness, perception of health and overall life situation in HD patients [37]. Forty eight HD patients who were free of any other systemic disease, and who each used two methods of exercise training for duration of one year, were studied. Half of the patients (Group A) were randomly assigned to a supervised outpatient exercise training program (three times weekly) on the non-HD days, whilst the other half (Group B) followed a training program with stationary bicycles during their HD sessions (3/weekly). The physical fitness and well-being parameters which were measured every year were: 1) aerobic capacity, as estimated from a modified treadmill exercise test and spiroergometric study, 2) the patients' perception of their health, 3) the overall life situation and 4) employment status [37]. During the study, there were 8 drop-outs in Group A and 5 in B. No adverse effects of the exercise programs were reported. The one year of exercise training resulted in 38% in group A (16 patients) and 31% in group B (18 patients) improving their exercise time, a 47% increase in Group A of peak oxygen consumption (VO₂peak) and a 36% in group B by comparison to the baseline value [37]. After three additional years of training, significant improvements were also noted in exercise time (by 53% in Group A and by 43% in B) and VO₂peak (by 70% in Group A and by 50% in Group B), as well as in other gas exchange variables in comparison to baseline values. However, the improvements in Group A were more pronounced than in B. Interestingly, the gains in exercise capacity were more enhanced in the first year of training in both groups. After four years of training, significantly more patients in both groups perceived their health and overall life situation as being improved compared to baseline. In addition, perception of improved health was higher in Group A. In conclusion, the study established that HD patients can adhere to long-term physical activity programmes on non-HD days, as well as during HD with considerable improvements in physical fitness and health [37].

Diet and Nutrition

HD patients have many concerns when it comes to eating the 'right food'. The diet of a HD patient is somewhat different to that of a patient post-transplant. Because the majority of HD recipients do not have adequate renal function, this will cause some parameters to be unstable, particularly creatinine (relatively high), urea (high), phosphate (high, controlled with phosphate binders and potentially parathyroidectomy), and calcium (unstable, but controlled with calcium supplement/s). Potassium is also important to keep in control because at abnormal levels will cause hyperkalemia, causing arrhythmia. Potassium is reduced within the first hour of HD and this combined with muscle contraction will mildly effect calcium stores. As for urea and creatinine, these will not increase in patients who partake in exhaustive exercise because—physical activity should decrease these parameters [18].

Post exercise, it's sensible to take in carbohydrates, so the body is able to maintain energy; it is important that protein is part of a HD patient's normal diet because this allows strength building (muscle mass) [18]. Protein is an element in specific food (all types of fish, meat, and chicken).

Muscle mass tends to be reduced in the elder HD recipient, because the diet of an older patient will differ from younger patients. Exercise should decrease urea, decrease sodium, decrease potassium, increase appetite and potentially red cell/Hb turnover with the aid of erythropoietin (EPO) prescription.

Discussion

The RRT patient will undergo various procedures and protocols; some being more traumatic than others. However, patients should challenge negative implications by being involved physical activity. Patients will not know how long they will be on either treatment forms and for this reason they should be encouraged (or prescribed) to get involved in fitness programmes, which has obvious benefits. The majority of literature in this article favors exercise for the dialysis patient because ultimately it can improve outlook. Exhaustive exercise does improve HD efficacy and ultimately it can aid in the run up and preparation for a renal transplant, but not all patients will be able to tolerate such advanced activity owing to longer-term effects of HD [38]. It seems obvious there are various ways that HD efficacy can be enhanced through physical activity [39,40]. Research has shown that physical activity increases the efficiency of HD by reducing tissue solute composition due to increased perfusion of the skeletal muscles [32]. Research has also identified that exercise during HD is a practicable new way to improve HD efficiency [33]. Though debatable, perhaps the counter argument to this is that patients should not exercise during HD because they may experience reduced oxygen as red cells are continuously being turned over and patients may become prone to cramping as a complication, which then leads to hypotensive episodes. Perhaps one of the main recommendations is thus to see that patients partake in physical activity before/in between their HD sessions or at least 2-4 hours before. In turn, patients will

find that they feel better and ultimately find this improves treatment efficacy and urea clearance. Patients would also feel more energized if exercise is routine.

Conclusion

Physical activity as part of routine RRT has various benefits and it is evident that more research contributing to physical activity/exercise in renal patients is needed [41]. More research and studies are prompting discussion [42,43]. However, when exploring the larger role of physical activity in this patient population, it is important to inter-relate biochemical and haematological parameters, thus allowing a better picture of how blood and chemistry can improve in patients undergoing a HD regimen. There are limited studies exploring haematology parameters in HD patients who partake in physical activity and this may be due to general understanding that most HD patients have low hemoglobin levels. The immune system also plays a role. With most patients having co-morbidities, it would otherwise be good to see more research that associates physical activity with endocrinology in patients with ESRD, (i.e. to understand how HD patients' and their parameters are affected with psychological stress and β -endorphins). Certainly more longitudinal and cross-sectional studies are required to inform future care and practices.

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